

P<sup>A</sup>TENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

|   |   |
|---|---|
| Date of mailing (day/month/year)<br>30 March 2001 (30.03.01)          |   |
| International application No.<br>PCT/US00/19543                       | Applicant's or agent's file reference<br>X-12592          |
| International filing date (day/month/year)<br>21 July 2000 (21.07.00) | Priority date (day/month/year)<br>29 July 1999 (29.07.99) |
| Applicant<br>BRINER, Karin et al                                      |   |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
02 February 2001 (02.02.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|   |  |
|---|--|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br>Zakaria EL KHODARY<br>Telephone No.: (41-22) 338.83.38 |
|---|--|

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

**RECEIVED**

To:  
  
R. Craig Trucker  
ELI LILLY AND COMPANY  
Lilly Corporate Center  
Indianapolis Indiana 46285  
ETATS-UNIS D'AMERIQUE

OCT 02 2001

ELI LILLY & COMPANY  
PATENT DIVISION

**PCT**

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year) 17.09.2001

Applicant's or agent's file reference  
X-12592

**IMPORTANT NOTIFICATION**

International application No.  
PCT/US00/19543

International filing date (day/month/year)  
21/07/2000

Priority date (day/month/year)  
29/07/1999

Applicant  
ELI LILLY AND COMPANY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|  |   |   |  |   |
|--|---|---|--|---|
| Applicant's or agent's file reference<br><b>X-12592</b>  |   | <b>FOR FURTHER ACTION</b>   |  | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No.<br><b>PCT/US00/19543</b>   | International filing date (day/month/year)<br><b>21/07/2000</b> | Priority date (day/month/year)<br><b>29/07/1999</b>                           |  |   |
| International Patent Classification (IPC) or national classification and IPC<br><b>C07D307/79</b>  |   |   |  |   |
| Applicant<br><b>ELI LILLY AND COMPANY et al.</b>   |   |   |  |   |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>  |   |   |  |   |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul> |   |   |  |   |
| Date of submission of the demand<br><b>02/02/2001</b>  |   | Date of completion of this report<br><b>17.09.2001</b>                        |  |   |
| Name and mailing address of the International preliminary examining authority:<br> <b>European Patent Office</b><br><b>D-80298 Munich</b><br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465  |   | Authorized officer<br><b>Ladenburger, C</b><br>Telephone No. +49 89 2399 8276 |  |   |



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/19543

**I. Basis of the report**

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

**Description, pages:**

1-106 as originally filed

**Claims, No.:**

1-6 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application; the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/19543

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3-6 as to IA.

because:

☒ the said international application, or the said claims Nos. 3-6 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |                 |
|-------------------------------|-----------------|
| Novelty (N)                   | Yes: Claims 2-6 |
|                               | No: Claims 1    |
| Inventive step (IS)           | Yes: Claims 1-6 |
|                               | No: Claims      |
| Industrial applicability (IA) | Yes: Claims 1,2 |

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/19543

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No: Claims

2. Citations and explanations  
see separate sheet

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/19543

**III. Non-establishment of opinion**

Claims 3-6 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**V.2 Reasoned statement: Citations and explanations**

1. The most relevant prior art documents cited in the ISR are:  
D1= WO-A-97/36893  
D2= EP-A-189 612  
D3= J. Med. Chem. (1995), 38, 1942-1954  
D4= US-A-5 698 766
2. A compound of formula I of claim 1 where A is homopiperazine has already been disclosed in D1: see D1, intermediate XI-H p.5 & 25/26. This particular subject-matter of claim 1 is therefore not novel.
3. Having regard to the fact that the prior art documents neither specifically disclose any other compound of formula I of claim 1 (the general formulae n p.30 of D1 and 1 p.21 of D2 overlap with formula I of claim 1, however, the most important parts of the overlapping areas, and especially the relevant individual compounds, as well as those described in D3, are disclaimed by means of provisos a, b and c) nor relate to 5-HT<sub>2C</sub> receptor agonists (except D4 wherein, however, the sole 5-HT<sub>2C</sub>R agonist mentioned, mCPP, presents a relatively important structural difference compared with the compounds of formula I), the subject-matter of claims 1-6, except the one of above point 2, can be considered as novel and inventive.
4. For the assessment of claims 3-6 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to th

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/19543

use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**VIII. Certain observations**

The provisos introduced in claims 1-5 should be clearly explained in the description (see e.g. Rule 5.1(a)(ii) PCT).



# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |   |  |
|---|---|--|
| Applicant's or agent's file reference<br><b>X-12592</b> | <b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |  |
| International application No.<br><b>PCT/US 00/19543</b> | International filing date (day/month/year)<br><b>21/07/2000</b>   | (Earliest) Priority Date (day/month/year)<br><b>29/07/1999</b> |
| Applicant<br><br><b>ELI LILLY AND COMPANY</b>           |   |  |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/19543

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D307/79 C07D405/04 C07D405/12 A61K31/496 A61P3/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| Y          | WO 97 08167 A (SMITHKLINE BEECHAM P.L.C.)<br>6 March 1997 (1997-03-06)<br>the whole document  | 1-6                   |
| Y          | KUIPERS W. ET AL: "N4-unsubstituted<br>n1-arylpiperazines as high-affinity 5-HT1A<br>receptor ligands"<br>JOURNAL OF MEDICINAL CHEMISTRY.,<br>vol. 38, no. 11, 26 May 1995 (1995-05-26),<br>pages 1942-1954, XP002153536<br>AMERICAN CHEMICAL SOCIETY. WASHINGTON., US<br>ISSN: 0022-2623<br>the whole document | 1-6                   |
| Y          | WO 97 36893 A (DUPHAR INTERNATIONAL<br>RESEARCH B.V.) 9 October 1997 (1997-10-09)<br>the whole document   | 1-6                   |

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

24 November 2000

Date of mailing of the international search report

13/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Beslier, L

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/19543

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                     | Relevant to claim No. |
|------------|--|-----------------------|
| Y          | EP 0 006 524 A (CIBA-GEIGY AG)<br>9 January 1980 (1980-01-09)<br>cited in the application<br>the whole document<br>--- | 1-6                   |
| Y          | WO 95 11243 A (SMITHKLINE BEECHAM P.L.C.)<br>27 April 1995 (1995-04-27)<br>the whole document<br>---                   | 1-6                   |
| Y          | EP 0 189 612 A (DUPHAR INTERNATIONAL<br>RESEARCH B.V.) 6 August 1986 (1986-08-06)<br>the whole document<br>---         | 1-6                   |
| A          | US 5 698 766 A (DAVID J. JULIUS)<br>16 December 1997 (1997-12-16)<br>cited in the application<br>-----                 |                       |

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/19543

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|---|---------------------|----------------------------|---------------------|
| WO 9708167                                | A | 06-03-1997          | NONE                       |                     |
| WO 9736893                                | A | 09-10-1997          | AU 708053 B                | 29-07-1999          |
|   |   |                     | AU 2029497 A               | 22-10-1997          |
|   |   |                     | BR 9708389 A               | 04-01-2000          |
|   |   |                     | CA 2250347 A               | 09-10-1997          |
|   |   |                     | CN 1215400 A               | 28-04-1999          |
|   |   |                     | CZ 9803068 A               | 13-01-1999          |
|   |   |                     | EP 0889889 A               | 13-01-1999          |
|   |   |                     | HU 9902471 A               | 28-03-2000          |
|   |   |                     | JP 2000507949 T            | 27-06-2000          |
|   |   |                     | NO 984533 A                | 02-11-1998          |
|   |   |                     | PL 329123 A                | 15-03-1999          |
|   |   |                     | SK 133198 A                | 11-02-1999          |
| EP 6524                                   | A | 09-01-1980          | AU 523656 B                | 05-08-1982          |
|   |   |                     | AU 4825779 A               | 03-01-1980          |
|   |   |                     | CA 1119601 A               | 09-03-1982          |
|   |   |                     | DD 144545 A                | 22-10-1980          |
|   |   |                     | DK 259879 A                | 23-12-1979          |
|   |   |                     | ES 481714 A                | 16-06-1980          |
|   |   |                     | ES 489627 D                | 01-04-1981          |
|   |   |                     | ES 8104280 A               | 01-07-1981          |
|   |   |                     | ES 489628 D                | 01-04-1981          |
|   |   |                     | ES 8104281 A               | 01-07-1981          |
|   |   |                     | JP 55002697 A              | 10-01-1980          |
|   |   |                     | NZ 190784 A                | 16-03-1982          |
|   |   |                     | US 4259338 A               | 31-03-1981          |
|   |   |                     | ZA 7903091 A               | 25-06-1980          |
| WO 9511243                                | A | 27-04-1995          | EP 0724580 A               | 07-08-1996          |
|   |   |                     | JP 9503773 T               | 15-04-1997          |
| EP 189612                                 | A | 06-08-1986          | AT 81975 T                 | 15-11-1992          |
|   |   |                     | AU 588015 B                | 07-09-1989          |
|   |   |                     | AU 5139185 A               | 26-06-1986          |
|   |   |                     | CA 1271475 A               | 10-07-1990          |
|   |   |                     | DE 3586794 A               | 10-12-1992          |
|   |   |                     | DE 3586794 T               | 27-05-1993          |
|   |   |                     | DK 586085 A                | 22-06-1986          |
|   |   |                     | ES 550104 D                | 16-12-1986          |
|   |   |                     | ES 8702143 A               | 16-03-1987          |
|   |   |                     | GR 853064 A                | 09-04-1986          |
|   |   |                     | IE 61723 B                 | 30-11-1994          |
|   |   |                     | IL 77395 A                 | 16-08-1991          |
|   |   |                     | JP 61152655 A              | 11-07-1986          |
|   |   |                     | NZ 214610 A                | 29-09-1988          |
|   |   |                     | PH 24503 A                 | 18-07-1990          |
|   |   |                     | US 5424313 A               | 13-06-1995          |
| US 5698766                                | A | 16-12-1997          | NONE                       |                     |